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# The difficult quest for data on “vanishing” vaccine-preventable infections in Europe: the case of measles in Flanders (Belgium)

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## Abstract

We aimed to describe the impact of vaccination on the epidemiology of measles infection in Flanders (Belgium), to document probable vaccination coverage based on this evidence, compare these epidemiological data with those generated by a mathematical model and estimate the costs of morbidity from measles. In contrast to previous analyses, we included the costs of long-term care for sequelae due to encephalitis and subacute sclerosing panencephalitis (SSPE). We estimated the direct health care costs per average measles case at € 227, 212, 210, 200 and 194 for the age groups of 0–4, 5–9, 10–14, 15–19 and ≥20 years, respectively. Excluding long-term care lowers these estimates by 22–51%, depending on the age group. By including indirect time costs, we arrive at total costs per measles case of € 320, 305, 210, 200 and 625, respectively. In addition to registering vaccination coverage more rigorously in the future, it seems necessary to undertake seroprevalence studies to document the age-specific immunity to measles. By using such information, current vaccination strategies can be adapted to prevent future outbreaks and to help eliminate measles from Europe in an efficient way. We noted throughout that many of the data sources are flawed. Better and accessible data bases are required to improve the reliability of similar studies in the future.


*Keywords:* Measles; Vaccination; Cost

## 1. Introduction

Measles is probably the most contagious infection in humans. In the absence of immunisation, the lifetime risk of infection is nearly 100%. Typical clinical symptoms include fever, coughing and rash. Less frequently measles can cause complications, such as conjunctivitis, diarrhoea, otitis media, pneumonia and encephalitis, or permanent disabilities, such as mental retardation, speech problems, deafness and blindness. Nowadays, measles is estimated to cause worldwide about 880,000 deaths annually [1] Since serious complications occur more often in low-income countries and in malnourished children, by far the largest part of todays' measles deaths occurs in sub-saharan Africa and India.

In Europe, following the introduction of mass vaccination, measles infection is no longer perceived as a major health threat. Nevertheless, whenever vaccination coverage falls to inadequate levels due to complacency or vaccine scare stories, outbreaks occur with sometimes lethal vigour. For instance in 2000, measles outbreaks caused two deaths in Dublin [2].

Since humans are the only hosts of the virus, measles could in theory be eradicated. It is estimated that 90–95% should be effectively immunised in order to halt transmission of the virus (this percentage is related to population density) [3]. The European office of WHO has issued an elimination goal for measles from its European member countries by 2007 [4].

In order to provide estimates of the marginal cost-effectiveness of increases in coverage and of appropriate timing of doses, economic evaluation studies of measles vaccination strategies are needed in Europe. To provide such evidence in Belgium, we need to collect accurate information on the current susceptibility profile of the population. This can be derived indirectly from data on vaccination coverage and case notifications through time combined with modelling exercises, or directly by randomised sero-prevalence surveys. Additionally, data on resource consumption associated with measles disease and vaccination are required. Such cost data were usually not assembled while the disease was still prevalent, implying that cost estimates are generally not available.

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Clearly, if we want to document the economic impact of measles elimination and eradication, such data are indispensable. In the following section we will subsequently review the available data on measles incidence and vaccination coverage in Belgium. In Section 3 we will make estimates of the direct and indirect costs of measles cases. Furthermore, estimates are made of marginal vaccination costs, specifically attributable to measles vaccination. The analysis is limited to the region of Flanders (about 60% of Belgium) for several reasons. Foremost, health prevention is a regional responsibility in Belgium and historically (due to differences in interventions and culture) most infectious diseases have evolved differently between the North (Flanders) and the South (Wallonia) of the country. Though the epidemiological data are therefore different, the costs per measles case are likely to be quite similar, and could be regarded as Belgian cost data.

## 2. Incidence of disease and coverage of vaccination

Measles vaccines became available on the Belgian market in 1975. Mass vaccination against measles started in 1982 with the combined measles-mumps rubella (MMR) vaccine, administered at the age of 15 months (in practice mostly between 12 and 18 months). From 1994 on, it was recommended to routinely administer a dose of MMR at the age of 11–12 years (which for most vaccine recipients would be a second dose). As such measles vaccination is included in the routine childhood vaccinations in Belgium, but it is not mandatory (of the current vaccinations, only polio vaccination is mandatory in Belgium).

The official Belgian incidence data are based on a sentinel network of about 150 general practitioners (GPs), about 85 of which (these numbers vary from year to year) are spread out over Flanders (age, sex and geographically representative). The data are collected and analysed by the national Scientific Institute of Public Health (SIPH). Measles cases are detected clinically only (no lab confirmation), based on: (1) typical exanthem; (2) fever and (3) one of the following: cough, coryza or conjunctivitis. Obvious disadvantages of the system are that small local outbreaks may be missed, that only cases presenting to GPs are included (no cases that go directly to a pediatrician or hospital) and that misdiagnosed cases are missed or erroneously included. It seems that the system is more likely to underestimate than to overestimate the true incidence of measles in Belgium. The incidence figures thus obtained are only an indicator of the trends over time, and should be treated with caution.

Like many other vaccines, widespread use of measles vaccines has three observable consequences in a population: (1) the incidence of clinical cases of measles strongly declines; (2) the average age at infection increases and (3) the interepidemic period increases [5].

As illustrated in Figs. 1 and 2, two of these effects have also been observed by the sentinel system in Flanders. The number of cases has decreased dramatically after the start

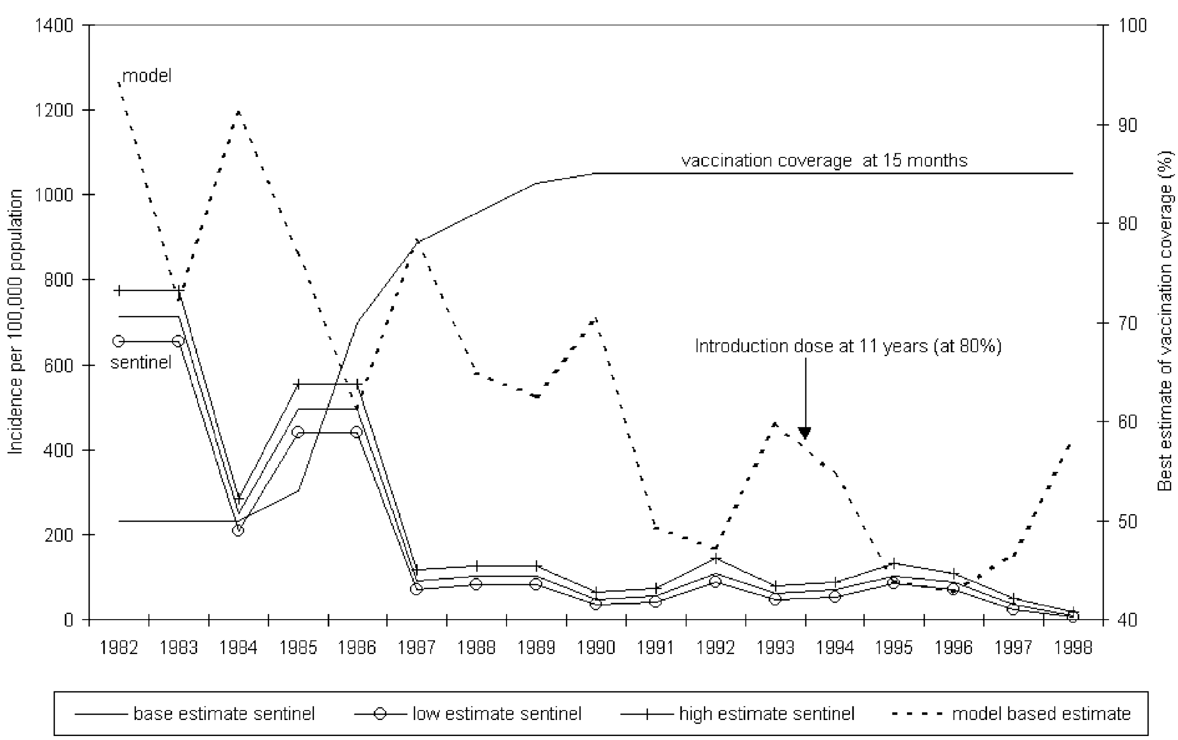


Fig. 1. Incidence of measles infection per 100,000 population and corresponding measles vaccination coverage in Flanders (Belgium). The annual data did not always conform to calendar years. It was assumed that the incidence data would average out over consecutive years if they bridged multiple calendar years (as was the case in 1982–1983, 1985–1986 and 1988–1989).

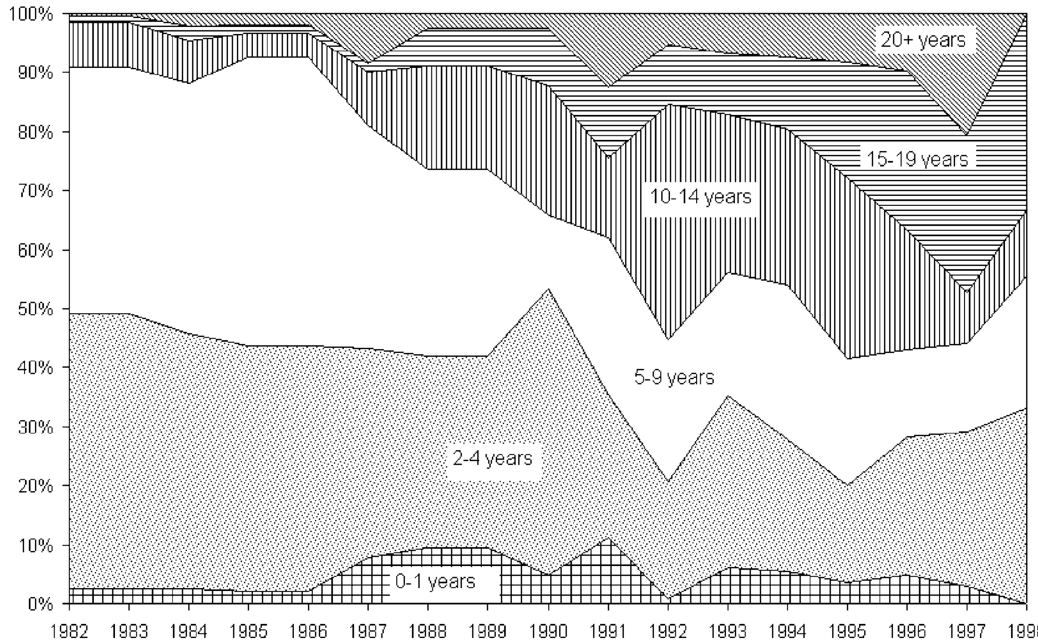


Fig. 2. Age distribution of measles cases reported through the sentinel system in Flanders (1982–1998).

of mass immunisation, from 714 per 100,000 population in 1982 to 10 per 100,000 population in 1998. The high and low estimates as reported by the SIPH (and depicted in Fig. 1), are based on a 95% CI around the mean, assuming a Poisson distribution. Only nine cases were registered by the sentinel system in 1998 and only one case in 1999 (not shown). As the sentinel system would become less reliable during periods that fewer people are infected and outbreaks occur at irregular intervals, data from the last 3 years seem far less reliable than data from previous years.

The evolution of the age distribution is given in Fig. 2 for six age groups. The general jagged outline of this figure seems indicative of the fragmented character of the surveillance system. Nonetheless the share of 5–9-year-olds clearly diminishes to the detriment of 15–19-year-olds, who are now more likely to be susceptible, because they grew up during the first years of the programme when coverage was relatively low. Due to the temporary cohort effect and the more fundamental decline in the force of infection, the average age at infection has steadily increased from 5.4 years in 1982 to 15.5 years in 1997 (see Fig. 3) [3]. In 1998, however, at 9.4 years the average age among the nine registered cases was much lower. The reliability of this estimate is highly questionable given the limitations of the system when cases are relatively few and clustered. The widening of the interepidemic period cannot be clearly determined from these data, though, we can suspect that it has increased from about 2 years prior to vaccination to about 4 years currently [5].

An accurate estimation of vaccination coverage over the years has proven to be equally problematic. The SIPH calculates vaccination coverage on the basis of the proportion of clinical cases of measles between the ages of 1 and 4 years who have a history of vaccination, by using an equation derived from Orenstein et al. [6]

$$V = \frac{C_v}{1 - E(1 - C_v)}$$

with $V$, vaccination coverage, $C_v$, proportion of the reported cases that are vaccinated, and $E$, protective vaccine efficacy. The SIPH assumed protective vaccine efficacy of 90%. In order to be able to use this formula in this way, one has to assume that the population between 1 and 4 years of age is totally susceptible if not vaccinated (i.e. people in this age group are assumed to become immune only through vaccination, and not by natural infection) and that vaccinated cases are as likely as unvaccinated cases to seek consultation. These assumptions greatly undermine the validity of these estimates.

The Well Baby clinics ("Kind & Gezin"), which vaccinate about 75% of infants <1 year have only partial data on vaccination coverage, that cannot be used in this context. The school health centres have recorded and analysed vaccination status in children aged 18–24 months from 1985 to 1993. Though these data are further recorded, they are not centralised and analysed every year. The data collected by the school health centres are seriously flawed because a large proportion of records is labeled unknown or missing (varying from 1 to 60% between reporting centres; 14% on average) [7]. Sales figures of vaccines are not fully available and can hardly be considered good estimators for vaccination coverage (the variable of interest is injected vaccines, not sold vaccines). Furthermore, sales figures refer to the whole of Belgium, and from the available data it is known that past vaccination coverage was markedly lower in the south of Belgium (Wallonia) than in Flanders. The most recent data suggest that this geographical gap is closing [8].

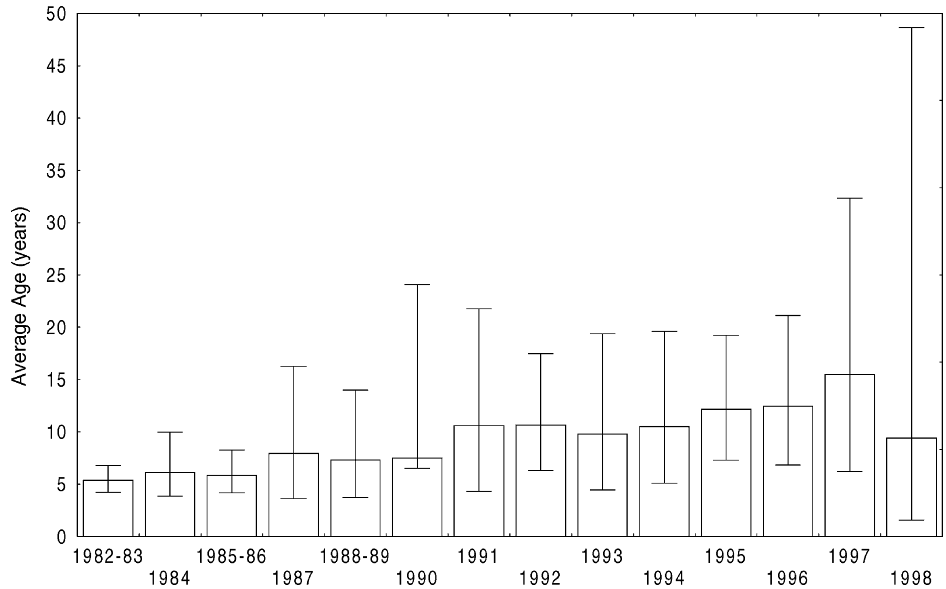


Fig. 3. Estimated average age at measles infection over time (years) and 95% CI, as reported through the sentinel system.

The most reliable vaccination coverage estimate was probably obtained in 1999, when coverage was determined by a representative cluster sample ($n = 1000$), in which parents of children between 18 and 24 months were asked about vaccination history, as confirmed by their personal vaccination booklet. The resulting coverage for measles was 83.4% [9]. In Fig. 4 the various coverage estimates are summarised, and a distinction is made between worst, best and base case estimates for each of the vaccination years. Smoothed base estimates of vaccination coverage (as depicted in Fig. 1 by the solid line) have been used to model the occurrence of infections with a deterministic age-structured dynamic model. This model has been validated in other European countries and should predict accurately the evolution of the number of cases over the years [10]. However, when the Flemish situation was modelled, using past and present coverage data for the first and second dose, and vaccine protective efficacy of 90%, the resulting number of infections (given by the dotted

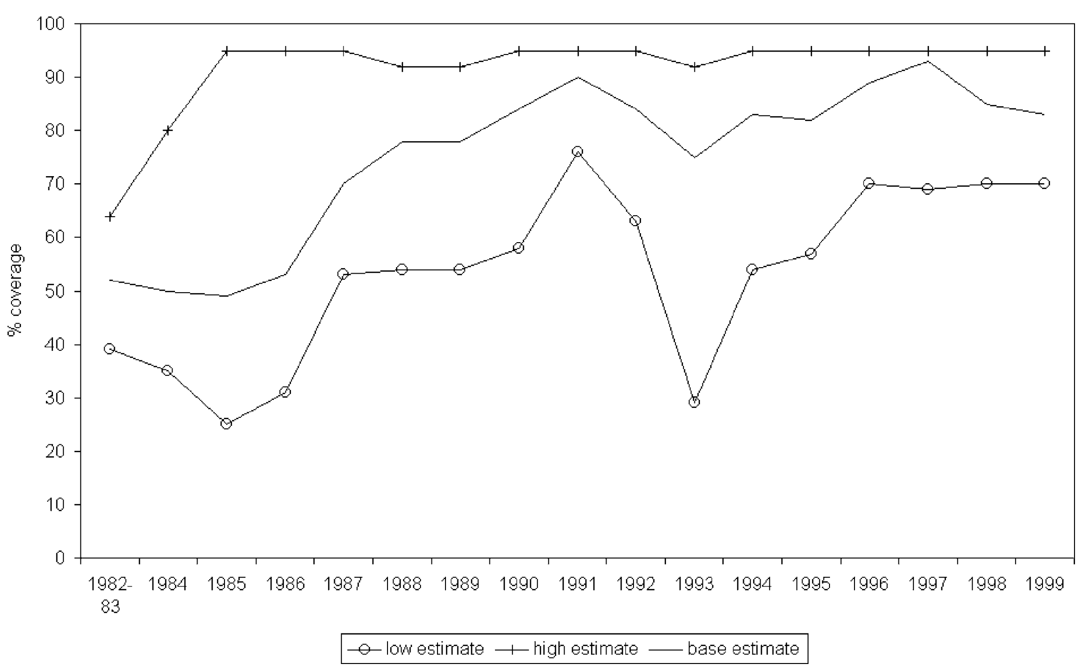


Fig. 4. Estimated coverage of measles vaccination at age 15 months in Flanders (1982–1999). Low and high estimates: 95% CI around the mean, on the basis of a Poisson distribution.

line in Fig. 1) is clearly much higher than cases observed by the sentinel system. It seems likely that the model slightly overestimates the number of cases, particularly when the infection is close to elimination (which is not the case at average vaccination coverage of 85% (see Fig. 1)). Given the limitations of the current surveillance system, it seems very likely that the case notifications provide an underestimation of the true incidence. Furthermore, the coverage data are only available up to the age of 2 years. In view of the great discrepancy between the observed number of cases and the number of cases predicted by the model, it seems likely that the true coverage of the first dose is substantially higher, possibly by complementary private vaccination between the ages of 2 and 10 years (by general practitioners, pediatricians and the school health centres). Therefore, in order to make a relevant analysis of measles vaccination strategies in Flanders, additional data are needed on first dose measles coverage in children >2 years of age. The role of second dose coverage (at the age of 11 years), though important to achieve elimination goals, has been shown to be less influential in the overall effectiveness and efficiency of a range of measles vaccination strategies [11].

Considering the unreliable nature of the existing data, it seems clear that seroprevalence surveys should be undertaken to establish the age-specific immunity.

## 3. Costs

### 3.1. Direct health care costs for measles

Assembling estimates on the health care costs of measles disease obviously becomes more problematic during periods that the disease is rare. Furthermore, the lack of any official and accessible database on hospitalisation data and health care costs of diseases is a serious impediment for independent research on any disease in Belgium. In 1999, we collected data on treatment costs by sending a short questionnaire to 279 Flemish general practitioners and pediatricians, of whom 101 (36%) responded. Forty-five responders had treated one or more cases of measles (no lab confirmation) during the previous 5 years. These responders were further asked about the treatment they provided for these measles patients. In this way we obtained data on the treatment of 146 patients (18%: <5 years; 18%: 6–11 years; 55%: 12–18 years; 8%: >18 years), from which age-specific treatment profiles were derived.

In Table 1 the average and median number of consultations (distinguishing between home and office visits) is given, as well as the average consultation costs per uncomplicated case. All costs presented in this paper are valued at the 1999 price level, and converted to Euro (€) (€ 1≅ US$ 1.07 (1999)).

Additionally, the mean costs of medication (mainly paracetamol and acetyl salisylic acid (and other antipyretics), eye

Table 1
Average number and costs of consultations per case of measles without complications

| Age class (years) | Office consultations mean (median) | Home visits mean (median) | Consultation costs per case mean (S.D.) (€ 1999) |
|---|---|---|---|
| 0–5 | 0.84 (0) | 0.92 (1) | 34.3 (13.9) |
| 6–11 | 0.52 (0) | 1.70 (2) | 45.9 (19.9) |
| 12–18 | 0.63 (1) | 1.59 (2) | 45.3 (17.9) |
| >18 | 1.17 (1) | 2.08 (3) | 65.1 (35.0) |

Average consultation costs per case based on the fixed 1999 day time tariffs of € 16.9 and 21.8 per office and home visit, respectively. The consultation costs per visit will never be lower, but they will be higher at night (21:00–08:00 h) and during weekends implying that the derived estimate can be regarded as conservative. These costs comprise national health insurance costs and patients' copayment.

droplets, nose droplets, and dextromethorphan) were estimated from the same sample at € 14.5 per uncomplicated case, irrespective of age.

The sample was too small to derive reliable estimates on age-specific complication and hospitalisation rates (overall six patients (4.1%) were hospitalised).

The following complications are most often reported in association with measles, and were included in the cost calculation: otitis media, bronchopneumonia, encephalitis and subacute sclerosing panencephalitis (SSPE). In Table 2 an overview is given of complication and hospitalisation probabilities per age group, based on previous studies in the UK and expert opinion [12–14]. The probabilities of hospitalisation (also for uncomplicated cases) were adjusted to be in accordance with recent overall (not per complication) age-specific hospitalisation probabilities in France (5.8, 1.7, 1.7, 1.6 and 5.3% for the age groups 0–4, 5–9, 10–14, 15–19 and ≥20 years), respectively (personal communication Daniel Lévy-Bruhl, 2000). In the absence of complications, it was estimated that 2.6, 0.4, 0.1, 0.6 and 3.7% of cases aged 0–4, 5–9, 10–14, 15–19 and ≥20 years, respectively, would be hospitalised.

In Table 2 the probability of a complication per age group is the first percentage, while the probability of hospitalisation conditional on the complication is in brackets. For instance, in the age group 0–4 years, the per-measles case probability of bronchopneumonia is 5.3%, whereas the probability of hospitalisation, given measles bronchopneumonia at that age, is estimated at 50%. There is considerable variety in the literature in the estimation of the per-case probability of encephalitis for age groups >9 years. Miller CL [12] (1978) did not find any neurological cases in these age groups, probably because the sample was too small. In a previous study, Miller DL [14] (1964) observed the probability of encephalitis at 0.38, 0.53 and 0.48% for the age groups 10–14, 15–19 and ≥20 years, respectively. The Centers for Disease Control [15] reported between 1973 and 1975 probabilities that increased linearly with age, similar to probabilities reported in England and Wales in 1980 [3]. However, in a more recent study for Canada, Pelletier et al. (1998)

Table 2
Estimated probability of complications (and hospitalisations, conditional on a particular complication)

| | Age class (years) | | | | |
|---|---|---|---|---|---|
| | 0–4 | 5–9 | 10–14 | 15–19 | ≥20 |
| Otitis media (%) | 3.8 (20) | 5.0 (1) | 5.0 (1) | 2.0 (1) | 2.0 (10) |
| Bronchopneumonia (%) | 5.3 (50) | 4.0 (30) | 5.0 (30) | 3.0 (30) | 3.0 (50) |
| Encephalitis (%) | 0.075 (100) | 0.1 (100) | 0.1 (100) | 0.1 (100) | 0.1 (100) |
| SSPE (%) | 0.0081 (100) | 0.0011 (100) | 0.0010 (100) | 0.0010 (100) | 0.0010 (100) |

SSPE: subacute sclerosing panencephalitis, in measles cases by age group. The values in parentheses are given in percentage.

estimated these probabilities much lower at 0.03 and 0.09% for the age groups 5–19 and ≥20 years, respectively [19]. In an attempt to give relatively more weight to the more recent studies, we attributed the same (most widely cited) risk of encephalitis (0.1%) to all age groups >4 years in the baseline. However, we also present alternative calculations with per case probabilities of encephalitis increasing with age (see below).

It was estimated that each complication would require four consultations, which have been distributed over office and home visits according to age in a similar fashion as the uncomplicated cases (Table 1). In addition to the medication mentioned above, cases of otitis media were calculated to cost in consumption of amoxicillin € 15.6, 31.2 and 39.7 for the age groups of 0–4, 5–9 and >9 years, respectively. For cases of bronchopneumonia, costs for similar medication (intravenous administration of amoxyclav) are added to the costs of one thorax X-ray, the costs of laboratory testing and the costs of physiotherapy to arrive at total medication and diagnostic costs of € 240, 279 and 300 for the age groups of 0–4, 5–9 and >9 years, respectively.

Based on the literature and expert opinion, we assumed that cases of encephalitis (or broadly similar other neurologic complications, such as meningitis) would be hospitalised for 9 days. Reported short-term lethality of encephalitis ranges from 10 to 30% [16]. The excess costs of long-term care for sequelae (e.g. mental retardation, speech retardation, deafness, blindness, epilepsy, hemiplegia, paraplegia), reported to occur in 20–30% of measles encephalitis cases are estimated at € 31,307 per year (taking into account that care for a handicapped person would cost on average € 34,835 per year whereas care for a normal person would cost € 3527 per year) [17,18]. This amount was summed and discounted over a 40 year period for children aged 0–4 years at the time of infection. For older age groups a proportionally shorter period of long-term care was taken into account (for ≥20 years old only 10 years). Thus, by discounting at 3%, we obtained a present value of € 723,662 for long-term care of sequelae per case at age 0–4 years down to € 267,058 at age ≥20 years. In our estimates we conservatively assumed that the case-fatality of measles encephalitis is 20%, and that long-term sequelae occur in 20% of surviving cases. By taking all these factors into account we arrive at total direct costs of € 118,240; 110,087; 100,636; 89,680; 45,183 per case of measles encephalitis, aged 0–4, 5–9, 10–14, 15–19 and ≥20 years, respectively. About 97% of these costs are for long-term care of sequelae.

SSPE is the rarest of serious measles complications, but also the most lethal one. It is characterised by personality changes, progressive deterioration of cerebral functions, myoclonus, paralysis, coma and death [13]. In a large follow-up study in the UK, the mean time interval between measles infection and clinical symptoms of SSPE was estimated at 8.2 years (range 3 months to 20.2 years). The median survival time from onset of SSPE to death was estimated at 1.8 years (ranging from 4 weeks to 16 years), with significantly shorter survival time if measles was contracted after the mean age of 2.4 years (1.1 years compared to 2.4 years) [13]. Based on the literature and expert opinion the average length of hospital stay due to SSPE is considered to be 11 days [19]. During the symptomatic period, we applied the same average excess costs of care as for encephalitis cases, namely € 31,307 per year. Intertemporal differences (the time intervals between infection and clinical manifestation and between clinical manifestation and death) were again taken into account by applying a discount rate of 3%. Thus, we arrived at a cost per case of SSPE of € 45,560. On average, the costs for SSPE are much lower than the costs for encephalitis (<20 years) because of the shorter time span between the onset of symptoms and death due to SSPE.

In summary, our estimates resulted in baseline direct health care costs per measles case of € 227, 212, 210, 200, 194 for the age groups of 0–4, 5–9, 10–14, 15–19 and ≥20 years, respectively. Table 3 shows alternative calculations, for both widely recommended discount rates (3 and 5%). Despite the relatively large discrepancies between these scenarios, we consider the baseline estimate (at a discount rate of 3%) to be the most relevant for the Flemish situation. There have been but a few studies that tried to estimate the health care costs of measles in Europe. These past studies included overall (non-age specific) direct cost estimates of € 145 per case <10 years in Spain (dating from 1981 to 1982) [20] and € 111 per case in Northern Ireland (dating from 1983) [21]. Neither of the published cost estimates from the past includes the costs of care for long-term sequelae (from neurological disorders like encephalitis and SSPE). Without the inclusion of long-term care, our cost estimates would become similar to the inflated past estimates given above (Table 3), lowering the original estimates by 22–51%, depending on the age group. In view of the

Table 3
Average direct costs per measles case by age using various scenarios (€ 1999)

| | Age class (years) | | | | |
|---|---|---|---|---|---|
| | 0–4 | 5–9 | 10–14 | 15–19 | ≥20 |
| Discount rate 3% | | | | | |
| Base | 227 | 212 | 210 | 200 | 194 |
| Low estimate[a] | 181 | 158 | 153 | 129 | 107 |
| High estimate[b] | 271 | 259 | 261 | 263 | 269 |
| Encephalitis age-dependent[c] | 185 | 267 | 311 | 379 | 375 |
| Canadian data[d] | 287 | 151 | 136 | 143 | 287 |
| No sequelae[e] | 136 | 103 | 112 | 113 | 151 |
| Discount rate 5% | | | | | |
| Base | 204 | 186 | 189 | 184 | 190 |
| Low estimate[a] | 165 | 141 | 141 | 121 | 107 |
| High estimate[b] | 243 | 226 | 231 | 238 | 257 |
| Encephalitis age-dependent[c] | 173 | 228 | 268 | 329 | 354 |
| Canadian data[d] | 266 | 143 | 130 | 138 | 283 |
| No sequelae[e] | 136 | 103 | 112 | 113 | 151 |

[a] Low estimate scenario: 30 years of long-term care for sequelae incurred at age 0–4 years (and proportionally adapted for older age groups, with no follow-up for individuals aged ≥20 years at infection) and consultation costs minus one standard deviation.

[b] High estimate scenario: 50 years of long-term care for sequelae incurred at age 0–4 years (and proportionally adapted for older age groups, with 20 years of follow-up for age groups older than 20 years at infection) and consultation costs plus one standard deviation.

[c] Encephalitis age-dependent: the probability of encephalitis was assumed to be a linearly increasing function of age (estimated as (age + 0.3265)/5599.5). For the oldest age group, the probability associated with age 30 years was retained (0.5%).

[d] Canadian data: based on probabilities of complications and hospitalisations as reported in Pelletier et al. [19]. All Flemish unit cost estimates (including the costs of long-term care) were retained.

[e] No sequelae: no costs attributed to long-term care for sequelae of encephalitis and SSPE.

current analysis it seems that the exclusion of the costs of long-term care could lead to substantial underestimation of the health care costs per measles case. However, it should be noted that the impact of these long-term costs may depend on the country's national health care system (and to which extent the health care sector (or society) finances such services). Furthermore, the fact that the relationship between age at infection and probability of encephalitis is not well understood introduces substantial uncertainty to the cost estimates, if long-term care is taken into account.

The average vaccination costs per dose (purchase costs and administration costs) specifically attributable to measles vaccination have been calculated at € 9.7. This calculation is based on the following assumptions: 71.6% of vaccinations occur through public channels, the remainder through private channels (32% GP, 56% pediatrician, 11% child care centres); when the vaccinator is a GP, 90% of vaccine is acquired at the public price and 10% at the private price, when the administrator is a pediatrician 95% of vaccine is bought at the public price and 5% at the private price; 95% of these private vaccinations are at the physician's office, 5% at the patient's home; 5% of vaccine goes wasted; the public price per dose is € 4.9; the private price per dose is € 9.4; vaccine associated adverse events are estimated at € 0.1 per dose (based on the reported association with high fever, thrombocytopenic purpura, anaphylaxis and febrile seizures) [22], the combined MMR vaccine is used for 98.5% and the measles monovalent vaccine for the remainder of vaccinations, the subjective importance of the measles component when given in the combined vaccine is assumed to be 50% (i.e. the incentive to increase coverage with the combined vaccine would be for 50% inspired by reducing future measles cases and for the other 50% for reducing mumps and rubella cases). The marginal costs for administering one extra vaccine dose was thus calculated at € 2.5 when done through the public channels (using physicians and nurses' time, approximately 15 min per shot) and € 9.8 by the private channels. Therefore, in addition to the price of the vaccine (which is minimally equal to the public price), the overall cost per extra dose is markedly greater through the private channels than through the public channels. Nonetheless, the private channels in Belgium are very important as they reach persons that would have remained unvaccinated. Mass non-mandatory vaccination in Belgium needs to be carried out by both channels in order to ensure sufficiently high coverage levels.

### 3.2. Indirect costs of time losses for measles

Although it is widely accepted that indirect costs in the form of time losses do represent some given quantity of costs (to the individual, to an employer, to society), current methods to measure that quantity are disputable [23,24]. Time losses arise whenever an individual interrupts his/her normal activities in society, because of illness or premature mortality (of him/herself or his/her relatives/friends), or to be subjected to an intervention, for instance, to be vaccinated. During the illness or for part of the rest of the expected lifetime (or very briefly during the vaccination consultation), this individual and society incur time costs.

Time losses associated with measles illness have not been investigated yet in Belgium, as in most European countries. Given the relatively rare occurrence of measles, carrying out such an analysis today imposes many difficulties. However, recently there have been analyses investigating the time losses associated with illness due to chickenpox (or varicella). In view of the fact that measles and varicella are broadly comparable (though in general varicella causes more benign illness than measles), it seems acceptable to use the estimated time losses and associated indirect costs for varicella as a proxy. In a recent economic evaluation of varicella vaccination in Belgium, these costs have been valued by a separate survey among 361 Belgian households with children between 0 and 12 years old [25]. Additional caretaking of the children did not cause practical problems, as long as one of the parents was not working full time or worked at home, or if the illness occurred during a holiday period. Otherwise, the grand parents (or occasionally other family members) were the most common minders of the sick

child (on average 1.89 days per child). Parents themselves took 0.58 days off work per average ill child. Furthermore a minder or baby-sitter was called upon for 0.58 days per average ill child. If the time of grand parents and baby-sitters are valued at the same price (the market price for general care taking of children) and the time of working parents is valued at the average gross earnings per day in Belgium we arrive at indirect costs of € 93.1 per varicella infected child. In view of the limited information for children aged >12 years, and the fact that these older children are likely to require less supervision, it seems acceptable to ignore indirect time costs for children aged 10 and more in the current analysis. Furthermore, it seems acceptable to assume that infected employed adults ≥20 years of age incur time costs for five working days. If we use these assumptions in combination with the direct costs for measles, we get total costs per measles case of € 320, 305, 210, 200 and 625, for the age groups of 0–4, 5–9, 10–14, 15–19 and ≥20 years, respectively.

## 4. Conclusion

No reliable data are readily available to determine the age-specific immunity to measles in the Flemish (and Belgian) population. Neither reported incidence, nor officially estimated vaccination coverage data seem sufficiently accurate for policy making when the disease in question has become rare. In view of this, a general sero-prevalence study is needed to establish accurately how and to which extent vaccination has impacted on the overall epidemiology of measles (and other infections). Such knowledge would allow targeting elimination strategies and preventing future outbreaks. The last documented outbreak of measles in Flanders occurred in 1996 (345 reported cases, 88% of which were between 10 and 20 years old) [26].

Morbidity related cost estimations of measles are very scarce. Yet in order to win public support for the elimination of measles from Europe in a first step and eradication of measles from the world in a second step, economic arguments will play an important role. Even if eradication would be considered undesirable in the face of recent political events, the relative efficiency of various control strategies (including elimination) would still be a topic of considerable interest. Evidently, the accuracy of measuring the economic impact of increased vaccination efforts depends very much on the accuracy of the estimated per case costs of measles. In this paper, we made an attempt to assess both the direct health care costs and the indirect costs of time losses per average case of measles. In contrast to previous direct cost estimates we included the costs of long-term care of sequelae due to encephalitis and SSPE. Our calculations yield a range between € 194 and € 227 per case, depending on the age at infection (with the youngest age group (0–4 years) giving rise to the most expensive, and the oldest age group (≥20 years) to the cheapest cases). Excluding long-term care lowers these estimates to € 103 and 151 (and makes cases in the oldest age group the most expensive, while teenage cases become the least expensive). If in addition to direct health care costs, indirect costs of time losses were included, the total costs per case of measles would range from € 200 to 625. If we apply these costs to the aforementioned outbreak, it seems that this would have costed € 70,322 to the health care payer and € 79,284 to society in Flanders (as in many other European countries, control measures for measles outbreaks are not recommended, and additional outbreak costs can therefore be ignored).

In sum, in this paper we tried to document the epidemiology and the costs of measles cases in Flanders. We have emphasised throughout the paper that some of the data sources are flawed and that there is substantial uncertainty about these estimates. Nonetheless, we have shown that the exclusion of long-term care for measles sequelae can lead to substantial underestimation of the total costs of measles disease. Furthermore, since the improvement of measles vaccination strategies may present savings to society as a whole, and not only to the health care sector, indirect costs of time losses should also be considered. These costs would add substantially to the costs per measles case in the youngest individuals (<10 years), as well as in adults.

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